

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Declaration for Patent Application

TKT91-02

As a named inventor, I hereby declare that

My residence, post office address and citizenship are as stated next to my name;

I believe I am the original, first and sole inventor (if only one name is listed) or an original, first and joint inventor (if plural names are listed in the signatory page(s) commencing at page 3 hereof) of the subject matter which is claimed and for which a patent is sought on the invention entitled

TARGETED INTRODUCTION OF DNA INTO PRIMARY OR SECONDARY CELLS

AND THEIR USE FOR GENE THERAPY

the specification of which (check one)

17 is attached hereto.

XX/ was filed on November 5, 1991 as
Application Serial No. 07/789,168 (if applicable).
and was amended on /

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to the examination of this application in accordance with Title 37, Code of Federal Regulations, §1.56(a).

I hereby claim foreign priority benefits under Title 35, United States Code, §119 of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate having a filing date before that of the application on which priority is claimed:

Prior Foreign Application(s)

**Priority
Claimed**

(Number) (Country) (Day/Month/Year filed)

(Number) (Country) (Day/Month/Year filed)

Yes

(Number) (Country) (Day/Month/Year filed)

I hereby claim the benefit under Title 35, United States Code, §120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35, United States Code, §112, I acknowledge the duty to disclose material information as defined in Title 37, Code of Federal Regulations, §1.56(a) which occurred between the filing date of the prior application and the national or PCT international filing date of this application:

(Application Serial No.) (Filing date) (Status, patented, pending, abandoned)

(Application Serial No.) (Filing date) (Status, patented, pending, abandoned)

As a named inventor, I hereby appoint the following attorney(s) and/or agent(s) to prosecute this application and transact all business in the Patent and Trademark Office connected therewith.

I also hereby grant additional Powers of Attorney to the following attorney(s) and/or agent(s) to file and prosecute an international application under the Patent Cooperation Treaty based upon the above-identified application, including a power to meet all designated office requirements for designated states.

David E. Brook	Registration No. 22,592
James M. Smith	Registration No. 28,043
Leo R. Reynolds	Registration No. 20,884
Richard A. Wise	Registration No. 18,041
Patricia Granahan	Registration No. 32,227
Mary Lou Wakimura	Registration No. 31,804
Thomas O. Hoover	Registration No. 32,470
Alice O. Carroll	Registration No. 33,542

all of Hamilton, Brook, Smith and Reynolds, P.C., Two Militia Drive, Lexington, Massachusetts 02173;

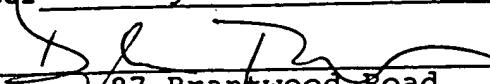
and

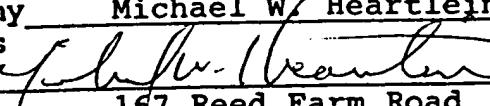
Send correspondence to: Patricia Granahan, Esq.
HAMILTON, BROOK, SMITH & REYNOLDS, P.C.
Two Militia Drive, Lexington, MA 02173

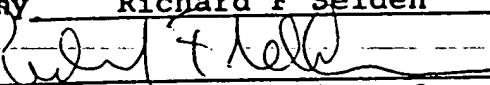
Direct telephone calls to: Patricia Granahan, Esq.

(617) 861-6240

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Full name of sole or first inventor Douglas Treco
Inventor's Signature  Date 1/2/92
Residence 87 Brantwood Road
Arlington, MA 02174
Citizenship U.S.A.
Post Office Address same as above

Full name of second joint inventor, if any Michael W. Heartlein
Second Inventor's Signature  Date 1/2/92
Residence 167 Reed Farm Road
Boxborough, MA 01719
Citizenship U.S.A.
Post Office Address same as above

Full name of third joint inventor, if any Richard F. Selden
Third Inventor's Signature  Date 01/02/92
Residence 106 Bristol Road
Wellesley, MA 02181
Citizenship U.S.A.
Post Office Address same as above

Full name of fourth joint inventor, if any _____
Fourth Inventor's Signature _____ Date _____
Residence _____
Citizenship _____
Post Office Address _____



UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
ASSISTANT SECRETARY AND COMMISSIONER
OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

DATE: 05/11/92
TO:
HAMILTON, BROOK, SMITH & REYNOLDS, P.C.
PATRICIA GRANAHAN
TWO MILITIA DR.
LEXINGTON, MA 02173-4799

COPY

RECEIVED

MAY 28 1992

HAMILTON, BROOK,
SMITH & REYNOLDS

UNITED STATES PATENT AND TRADEMARK OFFICE
NOTICE OF RECORDATION OF ASSIGNMENT DOCUMENT

THE ENCLOSED DOCUMENT HAS BEEN RECORDED BY THE ASSIGNMENT DIVISION OF
THE U.S. PATENT AND TRADEMARK OFFICE. A COMPLETE MICROFILM COPY IS
AVAILABLE AT THE U.S. PATENT AND TRADEMARK OFFICE ON THE REEL AND FRAME
NUMBER REFERENCED BELOW.

PLEASE REVIEW ALL INFORMATION CONTAINED ON THIS NOTICE. THE INFORMATION
CONTAINED ON THIS RECORDATION NOTICE REFLECTS THE DATA PRESENT IN THE
PATENT ASSIGNMENT PROCESSING SYSTEM. IF YOU SHOULD FIND ANY ERRORS, ON
THIS NOTICE, PLEASE SEND A REQUEST FOR CORRECTION TO: U.S. PATENT AND
TRADEMARK OFFICE, ASSIGNMENT BRANCH, NORTH TOWER BUILDING, SUITE 10C35,
WASHINGTON, D.C. 20231

ASSIGNOR: TRECO, DOUGLAS DOC DATE: 04/09/92

ASSIGNOR: HEARTLEIN, MICHAEL W. DOC DATE: 04/09/92

ASSIGNOR: SELDEN, RICHARD F. DOC DATE: 04/09/92

RECORDATION DATE: 04/17/92 NUMBER OF PAGES 004 REEL/FRAME 6083/0343

DIGEST :ASSIGNMENT OF ASSIGNORS INTEREST

ASSIGNEE:
TRANSKARYOTIC THERAPIES, INC., A CORP. OF DE
195 ALBANY ST.
CAMBRIDGE, MASSACHUSETTS 02139

SERIAL NUMBER 7-789188 FILING DATE 11/05/91
PATENT NUMBER ISSUE DATE 00/00/00



HAMILTON, BROOK, SMITH & REYNOLDS, P.C.

TWO MILITIA DRIVE
LEXINGTON, MASSACHUSETTS 02173-4799

(617) 861-6240

DAVID E. SMITH
JAMES M. SMITH
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ROBERT T. CONWAY
RICHARD B. SMITH
DOREEN M. HOGLE
KELLY MCKENNEY**
LAUREN E. JENSEN***

*PATENT AGENT
**NY BAR ONLY
***PA BAR ONLY

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service as First Class Mail in an envelope addressed to Honorable Commissioner of Patents and Trademarks, Washington, D.C. 20231 on 4/14/92

Hamilton, Brook, Smith & Reynolds, P.C.

Patricia Granahan
Signature

4/14/92
Date

April 14, 1992

MUNROE H. HAMILTON
(1906-1984)

OF COUNSEL
RICHARD A. WISE

OFFICE ADMINISTRATOR
BARBARA J. FORGUE

PATENTS, TRADEMARKS
AND COPYRIGHTS

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U.S. PATENT AND TRADEMARK OFFICE
4/14/92

The Honorable Commissioner of
Patents and Trademarks
Washington, D. C. 20231

Attention: Assignment Division

Re: Applicants: Douglas Treco et al.
Serial No.: 07/789,188
Filed: November 5, 1991
Title: TARGETED INTRODUCTION OF DNA
INTO PRIMARY OR SECONDARY CELLS AND THEIR
USE FOR GENE THERAPY
Docket No.: TKT91-02

Sir:

Please record the enclosed Assignment for the above-referenced patent application from Douglas Treco, Michael W. Heartlein and Richard F Selden to Transkaryotic Therapies, Inc., 195 Albany Street, Cambridge, MA 02139.

Authorization is granted to charge the recordal fee of \$40.00, and any additional fee which may be due, to Applicant's Attorney's Deposit Account No. 08-0380. A duplicate copy of this letter is enclosed for accounting purposes.

Respectfully submitted,


Patricia Granahan
Attorney for Applicants
Registration No. 32,227

Enclosure

PG/jzg

91620700

REEL 6083 FRAME 343

Assignment

WHEREAS, we, Douglas Treco, Michael W. Heartlein and Richard F Selden have invented a certain improvement in TARGETED INTRODUCTION OF DNA INTO PRIMARY OR SECONDARY CELLS AND THEIR USE FOR GENE THERAPY described in an application for Letters Patent of the United States, Serial No. 07/789,188, filed November 5, 1991.

WHEREAS, Transkaryotic Therapies, Inc. (hereinafter "ASSIGNEE"), a corporation organized and existing under the laws of the State of Delaware, and having a usual place of business at 195 Albany Street, Cambridge, Massachusetts 02139 desires to acquire an interest therein in accordance with agreements duly entered into with us;

NOW, THEREFORE, to all whom it may concern be it known that for and in consideration of the said agreements and of other good and valuable consideration, the receipt of which is hereby acknowledged, we have sold, assigned and transferred and by these presents do hereby sell, assign and transfer unto said ASSIGNEE, its successors, assigns and legal representatives, the entire right, title and interest in and throughout the United States of America, its territories and all foreign countries, in and to the said invention as described in said application, together with the entire right, title and interest in and to the said application and such Letters Patent as may issue thereon; said invention, application and Letters Patent to be held and enjoyed by said ASSIGNEE for its own use and behalf and for its successors, assigns and legal representatives, to the full end of the term for which said Letters Patent may be granted as fully and entirely as the same would have been held by us had this assignment and sale not been made; we hereby convey all rights arising under or pursuant to any and all international agreements, treaties or laws relating to the protection of industrial property by filing any such applications for Letters Patent. We hereby acknowledge that this assignment, being of the entire right, title and interest in and to said invention, carries with it the right in ASSIGNEE to apply for and obtain from competent authorities in all countries of the world any and all Letters Patent by attorneys and agents of ASSIGNEE selection and the right to procure the grant of all such Letters Patent to ASSIGNEE for its own name as assignee of the entire right, title and interest therein;

AND, we hereby further agree for ourselves and our executors and administrators to execute upon request any other lawful

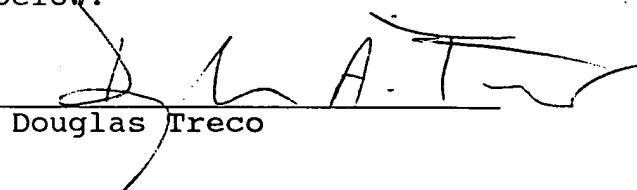
REF ID: A60831M34

documents and likewise to perform any other lawful acts which may be deemed necessary to secure fully the aforesaid invention to said ASSIGNEE, its successors, assigns and legal representatives, but at its or their expense and charges, including the execution of applications for patents in foreign countries, and the execution of substitution, reissue, divisional or continuation applications and preliminary or other statements and the giving of testimony in any interference or other proceeding in which said invention or any application or patent directed thereto may be involved;

AND, we do hereby authorize and request the Commissioner of Patents of the United States to issue such Letters Patent as shall be granted upon said application or applications based thereon to said ASSIGNEE, its successors, assigns, and legal representatives;

IN TESTIMONY WHEREOF, we have hereunto set our hands and affixed our seals the date set forth below.

Inventor:


Douglas Treco

State/Commonwealth

of Massachusetts
County of Middlesex

Then personally appeared before me the above-named Douglas Treco and acknowledged that he executed the foregoing instrument as his free act and deed this 8th day of April, 1982

(SEAL)

Frank M. Ventola Notary Public
FRANK M. VENTOLA (print name)
My Commission expires 10/04/90

REF 6083 FRAME 345

Inventor:

Michael W. Heartlein
Michael W. Heartlein

State/Commonwealth

of Massachusetts

County of Middlesex

Then personally appeared before me the above-named
Michael W. Heartlein and acknowledged that he
executed the foregoing instrument as his free act and
deed this 9th day of April, 1992.

Richard F. Selden Notary Public
(STAN) R. Selden (print name)
My Commission expires 10/04/96

Inventor:

Richard F. Selden

State/Commonwealth

of Massachusetts

County of Middlesex

Then personally appeared before me the above-named
Richard F Selden and acknowledged that he
executed the foregoing instrument as his free act and
deed this 9th day of April, 1992.

Richard F. Selden Notary Public
(STAN) R. Selden (print name)
My Commission expires 10/04/96.

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APR 17 1992

REEL 6083 FRAME 346

TKf91-02 TVS
PG39
PG/fzg
01-03-92

PATENT APPLICATION
Docket No. TKT91-02

COPY

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Douglas Treco, Michael W. Heartlein and
Richard F Selden

Serial No.: 07/789,168

Filed: November 5, 1991

Title: TARGETED INTRODUCTION OF DNA INTO PRIMARY
OR SECONDARY CELLS AND THEIR USE FOR GENE
THERAPY

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being
deposited with the United States Postal Service as First
Class Mail in an envelope addressed to Honorable
Commissioner of Patents and Trademarks, Washington,
D.C. 20231 on 12-12-91
Hamilton, Brook, Smith & Reynolds, P.C.

TRANSMITTAL OF VERIFIED STATEMENT CLAIMING
SMALL ENTITY STATUS AND REQUEST FOR REIMBURSEMENT

The Honorable Commissioner of
Patents and Trademarks
Washington, DC 20331
ATTN: APPLICATION BRANCH

Sir:

Transmitted herewith is a Verified Statement Claiming
Small Entity Status (37 C.F.R. 1.9 (f) and 1.27 (c))

- Small Business Concern, for filing in the above-identified application. Applicants' Attorney respectfully requests reimbursement of \$935, which represents one half of the filing fee paid (\$1870). The reimbursement is to be deposited in Deposit Account No. 08-0380. This request is made within the two-month period allowed for such reimbursement.

Two duplicate copies are enclosed for accounting purposes.

Respectfully submitted,

Patricia Granahan

Patricia Granahan
Registration No. 32,227
Attorney for Applicants
(617) 861-6240

Lexington, Massachusetts 02173

Date: January 4, 1992

Applicant or Patentee: Douglas Treco, Michael W. Heartlein and Richard F. Selden Attorney's
Serial or Patent No.: 07/789,168 Docket No.: TKT91-02
Filed or Issued: November 5, 1991
For: TARGETED INTRODUCTION OF DNA INTO PRIMARY OR SECONDARY CELLS AND THEIR USE FOR GENE THERAPY

VERIFIED STATEMENT (DECLARATION) CLAIMING SMALL ENTITY STATUS
(37 CFR 1.9(f) and 1.27(c) - SMALL BUSINESS CONCERN

COPY

I hereby declare that I am

the owner of the small business concern identified below:
 an official of the small business concern empowered to act on behalf of the concern identified below:

NAME OF CONCERN Transkaryotic Therapies, Inc.

ADDRESS OF CONCERN 195 Albany Street

Cambridge, MA 02139

I hereby declare that the above identified small business concern qualifies as a small business concern as defined in 37 CFR 121.12, and reproduced in 37 CFR 1.9(d), for purposes of paying reduced fees to the United States Patent and Trademark Office, in that the number of employees of the concern, including those of its affiliates, does not exceed 500 persons. For purposes of this statement, (1) the number of employees of the business concern is the average over the previous fiscal year of the concern of the persons employed on a full-time, part-time or temporary basis during each of the pay periods of the fiscal year, and (2) concerns are affiliates of each other when either, directly or indirectly, one concern controls or has the power to control the other, or a third party or parties controls or has the power to control both.

I hereby declare that rights under contract or law have been conveyed to and remain with the small business concern identified above with regard to the invention, entitled Targeted Introduction of DNA Into Primary Or Secondary Cells and Their Use For Gene Therapy by inventor(s) Douglas Treco, Michael W. Heartlein and Richard F. Selden

described in

the specification filed herewith
 application serial no. 07/789,168, filed November 5, 1991.
 patent no. _____, issued _____.

If the rights held by the above identified small business concern are not exclusive, each individual, concern or organization having rights to the invention is listed below* and no rights to the invention are held by any person, other than the inventor, who would not qualify as an independent inventor under 37 CFR 1.9(c) if that person made the invention, or by any concern which would not qualify as a small business concern under 37 CFR 1.9(d), or a nonprofit organization under 37 CFR 1.9(e). *NOTE: Separate verified statements are required from each named person, concern or organization having rights to the invention averring to their status as small entities. (37 CFR 1.27)

NAME _____

ADDRESS _____
[] INDIVIDUAL [] SMALL BUSINESS CONCERN [] NONPROFIT ORGANIZATION

NAME _____

ADDRESS _____
[] INDIVIDUAL [] SMALL BUSINESS CONCERN [] NONPROFIT ORGANIZATION

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JULY 10 1991

I acknowledge the duty to file, in this application or patent, notification of any change in status resulting in loss of entitlement to small entity status prior to paying, or at the time of paying, the earliest of the issue fee or any maintenance fee due after the date on which status as a small entity is no longer appropriate. (37 CFR 1.28(b))

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application, any patent issuing thereon, or any patent to which this verified statement is directed.

NAME OF PERSON SIGNING _____ Richard F Selden

TITLE OF PERSON OTHER THAN OWNER _____ Chairman, Board of Scientific Advisors

ADDRESS OF PERSON SIGNING _____ 195 Albany Street

Cambridge, MA 02139

SIGNATURE _____ DATE 010291